

A BIOMIMETIC APPROACH TO BENZOPHENANTHRIDINE
ALKALOID FROM PROTOBERBERINE ALKALOID

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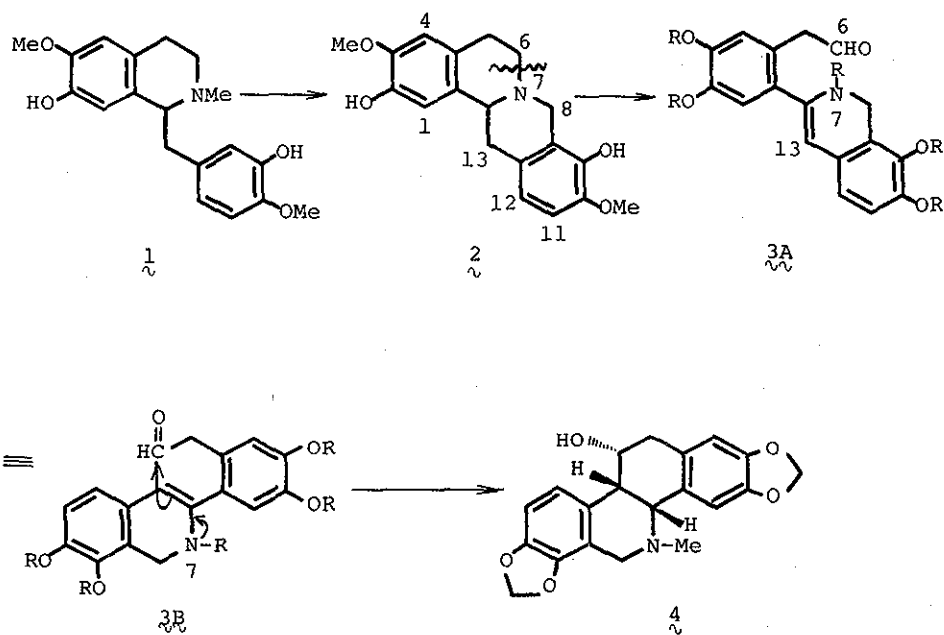
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10-Hydroxy-2,3,11-trimethoxyberbine (5) is transformed along by a biogenetic pattern into 7,8-dihydro-10-hydroxy-2,3,11-trimethoxybenzophenanthridine (11) via the methine base (6).

The benzophenanthridine alkaloids (4) are biosynthesised through cleavage of the C₆-C₇ bond of berbines (2), which are formed in plants from reticuline (1) type benzyloquinolines, followed by joining of C₆ to C₁₃ in 3 as shown in a biosynthesis of (+)-chelidonine (4).¹

Along this scheme Onda has synthesised benzophenanthridine alkaloids chelerythrine and sanguinarine by a photolytic electrocyclic reaction from the methine bases derived from protoberberines.² A similar type of reaction is applied in the synthesis of chelerythrine analog.³ We have also investigated a synthesis of benzophenanthridine alkaloids followed by a biogenetic line in connection with our previous work⁴ and here wish to report a novel formation of the benzophenanthridine (11) from the methine base (6) by a phenol oxidation.⁴

Scheme 1

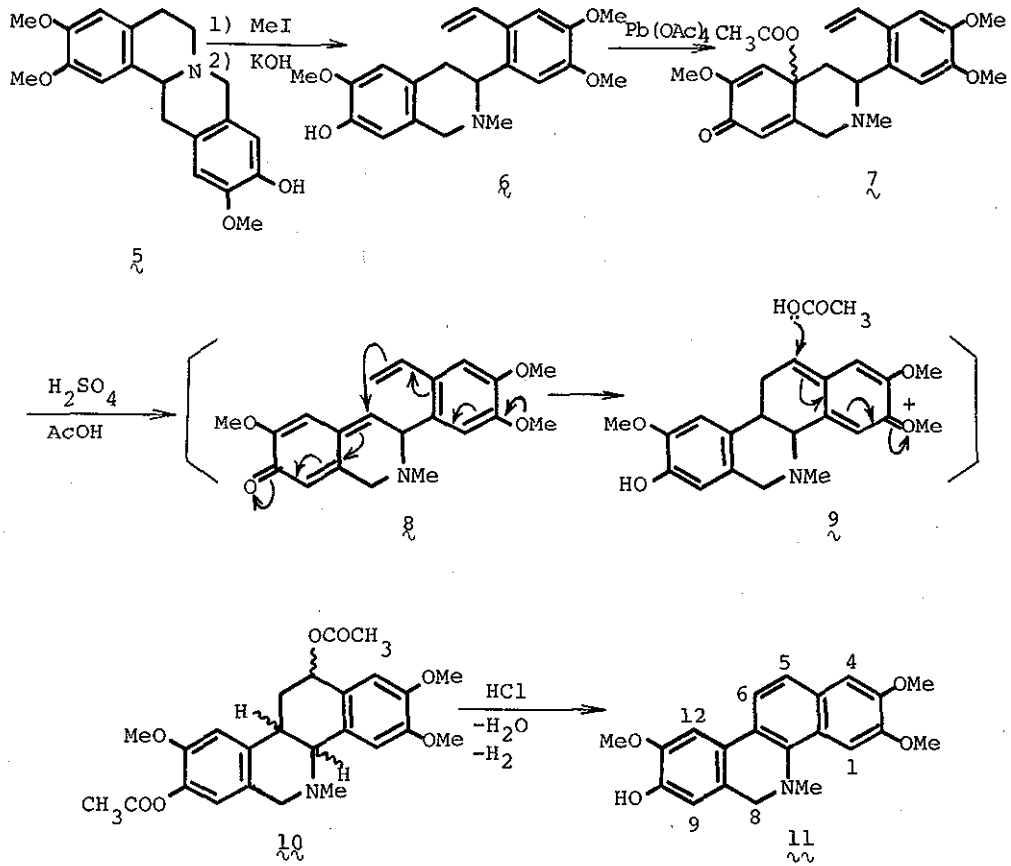


10-Hydroxy-2,3,11-trimethoxyberbine (5)⁵ methiodide, was subjected to Hofmann degradation with potassium hydroxide in methanol as usual⁶ to give the methine base (6) in a moderate yield,† m.p. 155 ~ 156°C [δ(CDCl₃) 2.16 (3H, s, NMe), 5.15 (1H, dd, J 2 and 11 Hz, CH=CH₂) and 5.50 (1H, dd, J 2 and 17 Hz, CH=CH₂)]. This was oxidised with lead tetraacetate⁷ in acetic acid at room temperature for 0.5 hr to afford the p-quinol acetate (7)[†] [ν_{max} (CHCl₃) 1743 (OCOCH₃) and 1680, 1658 and 1630 cm⁻¹ (dienone)], which without purification was treated with sulphuric acid in acetic anhydride at 0°, then at room temperature to furnish the benzophenanthridine derivative (10)[†] [ν_{max} (CHCl₃) 1760 and 1730 cm⁻¹]. Treatment of this product with hydrochloric acid in boiling ethanol gave 7,8-dihydro-10-hydroxy-2,3,11-trimethoxybenzophenanthridine (11)[†], m.p. 220° by a spontaneous dehydration and dehydrogenation of the initial product. This product showed a typical uv absorption [λ_{max} (EtOH) 312, 278, and 220 nm] of the benzophenanthridine system⁸ and a phenolic hydroxyl group at 3550 cm⁻¹. This structure was supported by the nmr spectrum revealing N-methyl at 2.60, three O-methyls at 3.97 (2 x OMe) and 4.06, methylene protons at 4.12 (s) and two vicinal aromatic protons at 7.47 and 7.70 as each doublet having J 8.0 Hz, in addition to four isolated aromatic protons at 6.84, 7.10, 7.27 and 7.67.

The formation mechanism is explained as follows. Intermediacy of the quinone methides (8) derived from the p-quinol acetate (7) would be responsible for the formation of benzophenanthridine (10) through 9 as shown in Scheme 2.

The methine bases having no hydroxyl group at C₇-position on the isoquinoline system are not transformed into the benzophenanthridine

Scheme 2



type of compounds by a treatment of lead tetraacetate or palladium chloride⁹.

This novel reaction seems to have general method for a synthesis of benzophenanthridine¹⁰ and we are now investigating a scope and application of our finding.

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